

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

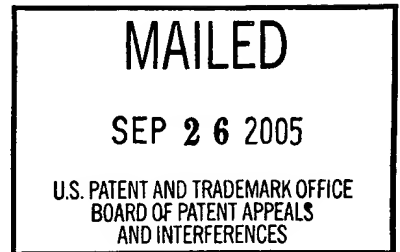
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte FELIX FRANKS and ROSS H. M. HATLEY

Appeal No. 2005-0847
Application No. 09/939,689

ON BRIEF



Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 26, 28, 29, 32-34, 38, 39, 41, 43, 46, 47, 52, and 54-68, which are all the claims pending in the application.

Claims 26, 38, 39, 52, 55, 56, 59, 60, 64 and 67 are illustrative of the subject matter on appeal and are reproduced below:

26. A glassy state composition which is storage-stable at 20° C, comprising:
- (1) a carrier substance which is water-soluble or water-swellaable and
 - (2) at least one material to be stored which is dissolved in said amorphous^[1] carrier substance;

¹ In the event of further prosecution, we encourage the examiner and appellants to work together to determine whether there is antecedent basis for the term "amorphous" as it appears in claim 26.

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C;

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1; and

wherein said biologically active material is not an enzyme.

38. A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said composition contains no more than 4 percent by weight of water; and

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous solution having a pH of about 7;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes and reductase enzymes.

39. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and is in a glassy state;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition exists in a glassy state at 20° C;
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;
wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;
wherein said composition contains no more than 4 percent by weight of water; and
wherein said biologically active material is not rennin.

52. A composition which is storage-stable at 20° C, comprising:
(1) a carrier substance which is water-soluble or water-swellaable and
(2) at least one material to be stored which is dissolved in said carrier substance;
wherein said composition has the property that it exists in a glassy state when at 20° C;
wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;
wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and
wherein said biologically active material is not freeze stable; and
with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.
55. A method of rendering a purified biologically active material storage-stable at 20° C and pharmacologically using said material, which material is unstable in aqueous solution at 20° C, comprising the steps of:
(1) dissolving to form an aqueous solution of
(a) a purified biologically active material (i) which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimmers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto and (ii) which is not an enzyme and

- (b) a carrier substance that is water-soluble or water-swellable;
 - (2) forming said solution into a glassy state composition by evaporating liquid water, wherein said glassy state composition exists when at 20° C; and
 - (3) administering said purified biologically active material stored in said glassy state composition.
- 56. The method of claim 55 wherein said purified biologically active material is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide.
- 59. The method of claim 55 wherein said purified biologically active material is an immunoglobulin.
- 60. The method of claim 55 wherein said purified biologically active material is a blood clotting factor.
- 64. A method of rendering a purified biologically active material storage-stable at 20° C, which material is unstable in aqueous solution at 20° C. comprising the steps of:
 - (1) dissolving to form an aqueous solution of
 - (a) a purified biologically active material, which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto and
 - (b) a carrier substance that is water-soluble or water-swellable;
 - (2) evaporating liquid water from said solution, thereby converting said solution to a glassy state composition, wherein said glassy state composition exists when at 20° C;
wherein said evaporating is done without heating; and
wherein said purified biologically active material is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide.

67. A glassy state composition which is storage-stable at 20° C, comprising:
- (1) a carrier substance which is water-soluble or water-swellaable;
 - (2) at least one material to be stored which is dissolved in said carrier substance;
- wherein said glassy state composition including said carrier substance has the property of being in a glassy state and being storage stable when at 20° C;
- wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C and is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide.

The reference relied upon by the examiner is:

Koyama et al. (Koyama)

4,824,938

Apr. 25, 1989

GROUND OF REJECTION

Claims 38, 39, 41 and 54 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification that fails to adequately describe the claimed invention.

Claims 38, 39, 41, and 54 stand rejected under 35 U.S.C. § 251 as based upon the introduction of new matter into the application for reissue.

Claims 26, 28, 29, 43, 46 and 52 stand rejected under 35 U.S.C. § 102(e) as anticipated by Koyama.

Claims 32-34, 47 and 55-68 stand rejected under 35 U.S.C. § 103 as being unpatentable over Koyama in view of appellants' admitted prior art.

We affirm the rejection of claims 38 and 54 under 35 U.S.C. § 112, first paragraph, and 35 U.S.C. § 251. We affirm the rejection of claims 26, 28, 29, 43 and 46 under 35 U.S.C. § 102(e). We affirm the rejection of claims 32-34, 47

and 55-68 under 35 U.S.C. § 103. We reverse the rejection of claim 52 under 35 U.S.C. § 102(e); and the rejection of claims 39 and 41 under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 251.

PROCEDURAL BACKGROUND

The instant application is a reissue application of United States Patent No. 5,098,893². According to appellants (page 2, Paper Received February 15, 2002), “[m]ore than one reissue application has been filed for the reissue of patent number 5,098,893. The reissue applications are application serial numbers 09/270,791, and application serial numbers 09/939,688³ and 09/939,689 [the instant application], which are continuation reissue applications of application serial number 09/270,791. Application number 09/270,791 has been allowed⁴.”

² For clarity, we recognize the examiner’s finding (page 2, Office Action, mailed December 4, 2002), “[t]he original patent was actually surrendered during the prosecution of the parent reissue application 09/270,791, and therefore the requirement set forth in 37 CFR [§] 1.178(a) has been satisfied.” In addition, we note the examiner’s finding (id.), “[t]he reissue declaration filed October 3, 2002 is approved.” We note, however, the examiner’s subsequent caution (bridging paragraph, pages 2-3, Office Action, mailed May 2, 2003), “in view of the subsequent amendments which have been made to this application, [a]pplicants are reminded of the likelihood that a supplemental reissue oath or declaration will have to be filed before this application can be allowed. See MPEP [§] 1444.”

³ This application issued as United States Patent No. RE38,385 on January 13, 2004. According to the examiner (Answer, page 2), the obviousness-type double patenting rejection in the instant application based upon Reissue Patent No. 38,385 “has been overcome by the terminal disclaimer filed July 3, 2003....”

⁴ See United States Patent No. RE37,872, issued October 8, 2002. According to the examiner (page 8, Office Action, mailed May 2, 2003), “[t]he obviousness-type double patenting rejection [in the instant application] based upon Reissue Patent No. 37,872 ... is overcome by the terminal disclaimer filed April 3, 2003, which has been approved.”

Appellants make the following statement (paragraph 14, Reissue Declaration, filed October 3, 2002), regarding the errors relied upon as the basis for reissue:

I rely upon the statement of the error in the originally filed parent reissue application No. 09/270,791 which is:

In original claim 12, a method claim, with a phrase “and forming the resulting mixture into a glassy amorphous state” arguably encompasses removing water from the mixture by sublimation, also known as freeze drying.

and the statement which is:

The applicants failed to claim a process “of forming a composition which is storage-stable at 20° C, said composition comprising the steps of:

- (1) dissolving to form an aqueous solution
 - (a) a carrier substance which is water-soluble or water-swellaable and
 - (b) at least one material to be stored;
- (2) evaporating liquid water from said solution to convert said solution into a composition in a glassy state;

wherein said composition has the properties that it is storage-stable and exists in said glassy state when at 20° C;

wherein said composition contains no more than 4 percent by weight of water;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C;

wherein said at least one material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said step of evaporating comprises heating the combined carrier substance and purified biologically active material to a temperature not exceeding 80° C”

TECHNICAL BACKGROUND

According to appellants' specification (column 1, lines 4-7⁵), "[t]his invention relates to the stabilization and storage of materials." Specifically, the claims before us on appeal are drawn to compositions, and methods of preparing compositions, comprising a biologically active material that is storage stable and exists in a "glassy state". Beginning at line 51 of column 3, appellants describe "THE GLASS-FORMING SUBSTANCE". According to appellants (specification, column 3, lines 52-60),

A glass is defined as an undercooled liquid with a very high viscosity....

Normally a glass presents the appearance of a homogeneous, transparent, brittle solid which can be ground or milled to a powder. In a glass, diffusive processes take place at extremely low rates, such as microns per year. Chemical or biochemical changes including more than one reacting moiety are practically inhibited.

According to appellants (specification, column 4, lines 57-60), "[c]arbohydrates are an important group of glass forming substances: thus candy is a glassy form of sugar.... The T_g for ... maltotriose ... [is] 76°C" According to appellants (specification, column 4, lines 12-15), "[f]or this invention it will generally be necessary that the glass forming substance, when anhydrous or nearly so, displays a glass transition temperature T_g in a range from 20 to 150°C " Once stored in a glassy state, the biologically active material may be recovered by "adding water or aqueous solution to a quantity of the glass with the active material therein." Specification, column 6, lines 61-63.

⁵ Since the instant application is a reissue application of United States Patent No. 5,098,893 ('893), all references to appellants' specification will be to the specification of the '893 patent.

DISCUSSION

Written Description:

Claims 38, 39, 41 and 54 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification fails to adequately describe the claimed invention.

Claims 38 and 54

According to appellants (Brief, page 10), claims 38 and 54 stand or fall together. Accordingly, we limit our discussion to representative independent claims 38. Claim 54 will stand or fall together with claim 38. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991). The examiner finds (Answer, page 4), claim 38 recites “dissolution in an aqueous solution having a pH of about 7, which embraces dissolution at slightly acidic pHs.” According to the examiner (id.), “there is no original disclosure in the specification of dissolution at slightly acidic pHs, the only pHs recited in the sections of the specification cited by [a]pplicants [is a pH] ranging from 7.0 to 7.6.” Accordingly, the examiner finds (id.), “the pH range recited in ... [claim 38] is not supported by the original disclosure of the invention.”

In response, appellants assert (Brief, page 12),

[w]hile the phrase “about 7” is not verbatim disclosed in the original specification, the claimed invention does not have to be described literally in the specification to satisfy the description requirement. The claim language “about 7” is a mere rephrasing of what the specification would have conveyed to one of ordinary skill in the art in view of the pH’s of the solutions actually disclosed. Therefore, the claimed phrase “pH of about 7” does not constitute new matter.

The examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention as defined by the claims. As the examiner explains (Answer, page 4), the phrase “having a pH of about 7” reads on a pH outside those pHs recited in appellants’ specification. Accordingly, it is our opinion that the examiner met his burden. In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). Therefore, appellants have the burden of demonstrating that the specification’s disclosure of pH 7.0, 7.5 and 7.6 provides written descriptive support for “a pH of about 7” as set for in appellants’ claim 38. While appellants assert, “a pH of about pH 7 is simply a rephrasing of what their specification would have conveyed to one of ordinary skill in the art,” they provide no evidence to support this assertion. It is not clear on this record, how a description of three specific pHs, pH 7.0, pH 7.5 and pH 7.6, describes about pH 7.0. See e.g., Answer, bridging paragraph, pages 7-8, “three specific pHs of 7.0, 7.5, and 7.6 do not convey that [a]ppellants contemplated the acidic pHs embraced by the claim language.”

For the foregoing reasons, we affirm the rejection of claim 38 under the written description provision of 35 U.S.C. § 112, first paragraph. As set forth above, claim 54 falls together with claim 38.

Claims 39 and 41

In the first action on the merits of the instant application, the examiner rejected then pending claims 17⁶, 19, 25, 40 and 42-44 under 35 U.S.C. § 102(b) as being anticipated by the Shah dissertation.⁷ In addition, the examiner rejected claims 26-29, 32-35 and 38 under 35 U.S.C. § 103 as being obvious over the Shah dissertation. See pages 11-13, Office Action, mailed June 3, 2002. According to the examiner (id. at page 11), "[t]he Shah dissertation teaches[, inter alia,] combining rennin, an enzyme, with preservatives such as gelatin (a synthetic polymer as well as a water soluble and a water-swellable synthetic polymer), dextrin, hydroxyethyl starch, and sucrose (a disaccharide) in an aqueous solution and spray-drying the aqueous solution." In the same Office Action, the examiner rejected claims 21, 31, 37-39 and 41 under 35

⁶ For clarity, then pending claim 17 is reproduced below:

17. A process of forming a composition which is storage stable at 20° C, said composition comprising the steps of:
- (1) dissolving to form an aqueous solution
 - (a) a carrier substance which is water-soluble or water-swellable and
 - (b) at least one material to be stored;
 - (2) evaporating liquid water from said solution to convert said solution into a composition in a glassy state;
 - wherein said composition has the properties that it is storage-stable and exists in said glassy state when at 20° C;
 - wherein said composition contains no more than 4 percent by weight of water;
 - wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C;
 - wherein said at least one material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and
 - wherein said step of forming comprises heating the combined carrier substance and purified biologically active material to a temperature not exceeding 80° C.

⁷ We note that an additional rejection of claims 17, 19, 25, 40 and 42-44 was made under 35 U.S.C. § 102(b) as being anticipated by the Shah dissertation further in view of Forshoff and appellants' admitted prior art at column 4, line 66 and column 5, lines 3-8. See page 12, Office Action, mailed June 3, 2002.

U.S.C. § 251, and 35 U.S.C. § 112, first paragraph, asserting “[t]here is no original disclosure supporting the exclusion of rennin as is recited in instant claims 21, 31, 37, 39, and 41.” See id., at pages 3-4.

According to the examiner (Answer, page 4), “[r]ennin is not mentioned in the disclosure, and silence in the specification is not support for a negative claim limitation.” Accordingly, the examiner finds (Answer, page 4), “[t]here is no original disclosure supporting the exclusion of rennin as is recited in instant claims 39 and 41.” In support of this rejection, the examiner relies on Ex parte Grasselli, 231 USPQ 339, aff’d on reh’g, 231 USPQ 395 (Bd. Pat. App. & Int. 1983).

In response, appellants admit (Brief, page 11), “the specification of this application does not mention rennin.” According to appellants (id.), the claims “specifically exclude[] rennin only because of the reference to rennin in the Shah reference.” Appellants assert, however, “that [this] does not mean that the applicant’s [sic] were not in possession of the genus of the inventions claimed by claims 39 and 41, either including or excluding rennin.” According to appellants (Brief, bridging paragraph, pages 11-12),

there is no rational basis for a rule of law precluding negative limitations that exclude a species anticipating a generic claim when the reference does not teach the generic utility of the claimed invention. That is the case here. To the extent case law is inconsistent with this reasoning, it should be overruled....

There can be no doubt that appellants have written descriptive support for a composition which comprises, inter alia, “peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes,

enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto..." as set forth in claims 39 and 41. See e.g., specification, column 2, line 63 to column 3, line 49. It is also clear that appellants' specification provides descriptive support for a subgenus within the genus of proteins that includes enzymes, transport proteins, e.g., haemoglobin, immunoglobulins, hormones, and blood clotting factors. See e.g., specification, column 3, lines 3-6. In addition, appellants specifically describe a number of enzymes including for example, the restriction endonuclease Eco RI (specification, Example 3), glutamate dehydrogenase (specification, Example 5), ascorbate oxidase (specification, Example 6), and Cytochrome C reductase (specification, Example 8).

As we understand the examiner's rejection, notwithstanding appellants' disclosure of a subgenus of proteins drawn to enzymes, and their specific disclosure of a number of enzymes within this subgenus, there is inadequate written descriptive support for appellants' claims that exclude the enzyme rennin. Apparently, it is the examiner's opinion that appellants have failed, per se, to provide adequate written descriptive support for claims that exclude the enzyme rennin, because "rennin" is not mentioned in appellants' specification.

We find the facts on this record to be substantially similar to those in In re Johnson, 558 F.2d 1008, 194 USPQ 187 (CCPA 1977). In Johnson, appellants narrowed their claims to avoid having them read on a lost interference count. On this record, appellants narrowed their claims to avoid

having them read on the prior art. As set forth in Johnson, at 1019, 194 USPQ at 196,

The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute.

The examiner failed to explain why after disclosing the genus - proteins, the subgenus – enzymes, and specifically describing several enzymes within the subgenus, that appellants have not described a composition as set forth in claims 39 and 41, wherein the biologically active material is not rennin. In our opinion, having described the whole, appellants have necessarily described the part remaining. Cf. id.

Accordingly, we reverse the rejection of claims 39 and 41 under 35 U.S.C. § 112, first paragraph.

New Matter:

Claims 38, 39, 41, and 54 stand rejected under 35 U.S.C. § 251 as based upon the introduction of new matter into the application for reissue. The rationale relied upon by the examiner to support the rejection of claims 38, 39, 41, and 54 stand rejected under 35 U.S.C. § 251 is exactly the same as rationale the examiner provides for the rejection under 35 U.S.C. § 112, first paragraph. In addition, appellants assert (Brief, page 21), the rejection under 35 U.S.C.

§ 251 “should be reversed for the same reasons stated in response to the rejection of claims under 35 U.S.C. [§] 112[, first paragraph].”

Claims 38 and 54

For the foregoing reasons, we affirm the rejection of claims 38 and 54 under 35 U.S.C. § 251, for the same reasons set forth above with regard to the rejection under 35 U.S.C. § 112, first paragraph.

Claims 39 and 41

For the foregoing reasons, we reverse the rejection of claims 39 and 41 under 35 U.S.C. § 251, for the same reasons set forth above with regard to the rejection under 35 U.S.C. § 112, first paragraph.

Anticipation:

Claims 26, 28, 29, 43, 46 and 52 stand rejected under 35 U.S.C. § 102(e) as anticipated by Koyama. According to appellants (Brief, page 10), claims 26, 28, 29, 43 and 46 stand or fall together. Claim 52 stands or falls alone. Accordingly, we limit our discussion to representative independent claims 26 and 52. Claims 28, 29, 43 and 46 will stand or fall together with claim 26. Young.

Claim 26

According to the examiner (Answer, page 4), Koyama “teach[es] stabilized water-soluble dry solid compositions comprising proteinaceous bioactive

substances, for example hormones. Aqueous solutions of the proteinaceous bioactive substances are combined with aqueous solutions [of] a polysaccharide composed mainly of maltotriose units at a ... weight ratio of the polysaccharide to the substance ... [of] at least 0.5....” The examiner finds (id.), “[t]he combined solutions are then dried, either by conventional procedures at reduced pressure and a temperature below 30°C, or else by freeze-drying.” The examiner further finds (id.), “[i]n one series of examples, greater than 90% of activity is retained after storage at 37°C for one month....”

Based on this evidence, the examiner concludes (Answer, bridging paragraph, pages 4-5), “[i]n view of the similarity in the components of the compositions and the retained activity of the compositions, the compositions of Koyama ... are deemed inherently to have the same storage stability ... claimed by [a]pplicants....”

Claim 26 is drawn to a “glassy state composition which is storage-stable at 20° C.” Claim 26 is not drawn to a particular method of forming a so-called “glassy state composition,” nor is does it include any process limitations relating to the formation of a glassy state composition. Therefore, the claims read on a glassy state composition that is storage-stable at 20° C, produced by any method.

Against this backdrop, we take a closer look at the evidence of record.

First: Koyama teach a composition that comprises a polysaccharide mainly composed of repeating maltotriose units, specifically pullulan and elsinan. See e.g., Koyama, abstract; Accord, Answer, page 4. There is no

dispute on this record that a polysaccharide mainly composed of repeating maltotriose units, e.g., pullulan and elsinan are not water-soluble or water-swallowable. Therefore, as we understand it, Koyama teaches a carrier substance as described in numbered clause (1) of appellants' claim 26.

Second: Koyama teaches non-enzyme proteins dissolved in the carrier substance. Koyama, Examples 1 through 7; Accord, Answer, page 4. There is no dispute on this record that the non-enzyme proteins taught by Koyama are not biologically active materials that are unstable in aqueous solution at 20° C. Therefore, as we understand it, Koyama teaches a purified biologically active material as described in the first, second and last wherein clause, as well as, numbered clause (2) of appellants' claim 26.

Third: Koyama teaches "[t]he weight ratio of the polysaccharide to the substance is at least 0.5...." Koyama, column 2, lines 44-45; Accord, Answer, page 4. Therefore, as we understand it, Koyama teaches a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1, as set forth in the fourth wherein claims of appellants' claim 26.

Fourth: Koyama teaches the dry solid obtained by following the teachings of their specification "is readily dissolvable in water, and very stably retains the activity of a proteinaceous bioactive substance." Koyama, column 2, lines 60-62; Accord Answer, page 4. In this regard, we note that Koyama demonstrates that a dry solid composition comprising e.g., pullulan and human IFN retained 100% of its activity after storage at 37° C for two months. Koyama, Experiment

1-B and Table 1, bridging columns 3-4; Accord, Answer, page 4. Therefore, as we understand it, Koyama teach a composition that has the properties that it is storage stable at 20° C, as set forth in the preamble and third wherein clause of appellants' claim 26.

Fifth: Koyama does not use the term "glassy state" to characterize his dry composition. We note, however, that appellants disclose (column 4, lines 12-15) "[f]or this invention it will generally be necessary that the glass forming substance [e.g., a maltotriose-based carrier], when anhydrous or nearly so, displays a glass transition temperature T_g in a range from 20 to 150° C." With reference to L. Slade and H. Levine, Non-equilibrium behavior of small carbohydrate-water systems, Pure Appl. Chem. 60[:]1841 (1988), appellants' disclose (column 4, lines 59-63), "[t]he T_g for ... maltotriose ... [is] 76° C." Thus, the T_g for maltotriose is within the range disclosed by appellants to be generally necessary to form a glass. There is no evidence on this, nor is there any dispute, that the maltotriose-based polysaccharides pullulan and elsinan would not have a T_g in a range from 20 to 150° C.

Based on the foregoing, it is our opinion that since the claimed and prior art products contain the same ingredients and can be produced by identical or substantially identical processes, they would have similar properties, including existing "in a glassy state." Therefore, it is our opinion that the examiner has set forth the evidence necessary to establish a prima facie case of anticipation, and thereby shift the evidentiary burden to appellants under the principles set forth in

In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977),

[w]here, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.... Whether the rejection is based on “inherency” under 35 U.S.C. 102, or “prima facie obviousness” under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO’s inability to manufacture products or to obtain and compare prior art products [citations and footnote omitted].

When the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicants have the burden of showing that they are not. In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). As set forth in In re Swinehart, 439 F.2d 210, 212-213, 169 USPQ 226, 229 (CCPA 1971)

It is elementary that the mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to those things to distinguish over the prior art. Additionally, where the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.

We now consider appellants’ rebuttal evidence.

First: appellants assert that Koyama “does not disclose any freeze drying conditions.” Brief, page 13. Apparently, appellants are of the opinion that a person of skill in the art would not understand how to perform a freeze-drying process. However, as appellants recognize (appellants’ specification, column 1, lines 29-66), “[t]he commonest method for the stabilization of isolated protein

preparations is freeze-drying.” We also note that this section of appellants’ specification provides a brief review of the known process known as freeze-drying. Accordingly, we are not persuaded by appellants’ intimation that anything more than routine steps, known to those in the art at the time of Koyama’s disclosure are required to perform the freeze-drying process according to Koyama’s disclosure.

Second: appellants assert (Brief, page 13), Koyama teach that the non-maltotriose based stabilizers⁸, otherwise referred to on this record as ineffective stabilizers⁹, do not provide high stability. From this appellants assert (Brief, page 14), “[i]f Koyama’s drying conditions resulted in the glassy state, all of Koyama et al.’s samples would have been stabilized....” In support of this assertion appellants direct our attention to the results obtained for compositions comprising dextran as the carrier substance as taught by appellants and Koyama. According to appellants (id.), Koyama’s dextran stabilized compositions “retained only 65.3% ... activity after being stored for two months at 37° C.” In contrast, appellants assert that their dextran stabilized compositions “exhibit greater than 91% activity when stored at 25° C for 8 and 10 weeks, respectively.” Id.

A closer look at the data is necessary to clarify appellants’ assertions. To begin, however, we do not understand Koyama to teach that compositions

⁸ We note that the terms “stabilizer(s)” and “carrier” are used interchangeably on this record.

⁹ See e.g., Answer, page 8, wherein the examiner distinguishes Koyama’s “ineffective stabilizers”, from Koyama’s “inventive polysaccharides,” those composed of repeating altotriose units, such as pullulan and elsinan. See e.g., Koyama, Abstract, and column 2, lines 37-41.

comprising non-maltotriose based carriers are not stabilized. Instead, we understand Koyama to teach that non-maltotriose based stabilizers do not stabilize a biologically active material as well as compositions comprising maltotriose based carriers.

In addition, while appellants emphasize the retention of a particular amount of activity, claim 26 simply requires that the composition be “storage stable.” There is no requirement in claim 26 that a particular amount of activity be retained during storage. We also find no disclosure in appellants’ specification that would define “storage stable” as having a particular amount of retained activity. Stated differently, we find no nexus between “[a] glassy state composition which is storage-stable at 20° C” and the retention of a particular amount of activity.

Nevertheless, we will consider appellants’ argument regarding activity. While appellants focus our attention only on the dextran data provided in their specification and in Koyama, we elect to consider both the dextran and the maltotriose data found in both appellants’ specification and in Koyama. In this regard, we note that appellants report (appellants’ specification, Table at column 13) that for compositions stored at 25° C the retained activity of,

1. maltotriose (114%) was better than dextran (81%) at week 2.
2. maltotriose (91%) was better than dextran (71%) at week 4.
3. maltotriose (96%) was better than dextran (89%) at week 6.
4. maltotriose (101%) was better than dextran (95%) at week 12.
5. maltotriose (94%) was better than dextran (84%) at week 16.

This is completely consistent with the observation in Koyama wherein, for example, the maltotriose-based carriers pullulan and elsinan stabilized human IFN better than dextran when stored at 37° C for two months (retained activity of pullulan 100% and elsinan 99.1% vs. dextran 65.3%). See Koyama, Table I, bridging columns 3 and 4).

There is no doubt that appellants' table reports an inversion in the general trend that maltotriose is a better stabilizer than dextran at weeks 8 and 10. See e.g., id., wherein at week 8 dextran based compositions retain 102% of their activity relative to maltotriose based compositions retaining 68%. Appellants offer no explanation for, nor do they even recognize, this inversion in the general trend reported in their Table. Accordingly, in the absence of evidence to the contrary, we consider the data presented for weeks 8 and 10 to be outliers, which are inconsistent with the general trend reported for the stabilization of compositions with either maltotriose or dextran for weeks 2-6, 12 and 16 as reported in their data. Therefore, we are not persuaded by appellants' assertion that because their data reports a different result for weeks 8 and 10 than is reported by Koyama, the products must be different. In our opinion, the evidence of record does not support this conclusion.

Therefore, we disagree with appellants' assertion (Brief, page 14), "[t]he only reasonable conclusion to draw from these facts is that Koyama's dextran containing samples were not in a glassy state." To the contrary, for the reason set forth above, we find it reasonable to conclude that the data set forth in appellants' table for weeks 8 and 10 is affected with some sort of experimental

error, which caused an inversion over the general trend set forth in the data, and causing dextran based compositions to retain more activity (102%, for week 8), than they originally started with.

For the foregoing reasons, it is our opinion that appellants failed to carry their burden to refute the examiner's prima facie case of anticipation.

Accordingly, we affirm the rejection of claims 26 under 35 U.S.C. § 102(e) as anticipated by Koyama. As set forth above, claims 28, 29, 43 and 46 fall together with claim 26.

For his part, the dissent agrees (infra, page 35) that Koyama supports a prima facie case of obviousness (see infra, page 26) with respect to claims 55, 56, 59, 60, 64 and 67, because Koyama suggests stabilizing "proteinaceous bioactive substances...." The dissent disagrees, however, that Koyama anticipates claim 26, because claim 26 "is directed to a 'glassy state composition.'" We respectfully point out that claims 55, 56, 59, 60, 64 and 67 also require a "glassy state" composition. See e.g., claim 55, step (2). Accordingly, as we understand it, the dissent's underlying rationale for distinguishing the claims appears to be flawed.

Nevertheless, we agree with the dissent that appellants' specification describes a process of making a glassy state composition that is an alternative to freeze-drying. See infra, page 39. However, while appellants' specification describes an alternative process to freeze-drying, there is no evidence on this record that the glassy state composition as set forth in claim 26 and described in appellants' specification cannot be prepared by freeze-drying. Appellants

appear to recognize this in their Reissue Declaration (filed October 3, 2002, paragraph 14), with regard to method claim 12 of the originally filed reissue application appellants assert the phrase “‘forming the resulting mixture into a glassy amorphous state’ arguably encompasses removing water from the mixture by sublimation, also known as freeze drying.”

The dissent attempts to distinguish freeze-drying from appellants’ alternative process of producing a “glass state” composition by emphasizing (infra, page 38) appellants’ description of their alternative process as, more “cost effective” than freeze-drying (column 2, lines 21-23), more energy efficient than freeze-drying (column 2, lines 60-61), and “more economical than freeze-drying” (column 4, lines 27-29). We fail to see, however, how statements relating to cost, and efficiency demonstrate that freeze-drying, as taught by Koyama and discussed above, does not result in a glassy state composition.

Nevertheless, the dissent directs our attention to example 13 of appellants’ specification in an attempt to support his opinion that freeze-drying will not result in a glassy state composition. At the outset, we note that the biologically active material of appellants’ example 13 is an enzyme – lactate dehydrogenase. Enzymes, however, are specifically excluded from the scope of claim 26. See claim 26, last clause. In addition, while the dissent recognizes (infra, page 39) that example 13 discusses “several different carriers” including maltotriose, the dissent limits his focus to “dextran”, and more specifically to the data for week 8, wherein the enzyme stabilized in dextran retained more activity than it originally started with. We find it curious, however, that like appellants

the dissent offers no explanation regarding, for example, the retained activity of the enzyme in dextran at weeks 2 and 4 (81% and 71% respectively), which is significantly less than the enzyme's retained activity at week 8 (102%). Stated differently, the activity of the enzyme appears to decrease when stored in a "glassy state" in dextran, up to week 8 wherein the activity of the enzyme exceeds it's original activity.¹⁰ Nevertheless, for the reasons set forth above, we are not persuaded by the dissent's focus on dextran, or the data presented in appellants' example 13 to distinguish the claimed "glassy state" composition, from the composition taught by Koyama.

We recognize the dissent's reference to the definition of a "glass" as it appears in column 3, lines 52-64 of appellants' specification. Infra, page 35. In particular, we note the dissent's reference to the glass transition temperature (T_g). According to appellants' specification (column 4, lines 12-15), "[f]or this invention it will generally be necessary that the glass forming substance, when anhydrous or nearly so, displays a glass transition temperature T_g in a range from 20 to 150° C...." We respectfully point out that maltotriose has a T_g of 76° C, well within the T_g range disclosed by appellants. Accordingly, since the components of the composition are the same and the process for preparing the composition can be the same, there is no evidence on this record that different results will be obtained.

¹⁰ We disagree with the dissent's intimation (infra, page 39) that the only meaningful data presented in appellants' table is the data for week 8, thereby ignoring the evidence of record that provides context for this single data point.

Accordingly, we are not persuaded by the dissents' attempt to distinguish Koyama's composition from the composition set forth in appellants' claim 26.

Claim 52

Claims 52 stands of a different footing. As illustrated above, claim 52 requires that "said biologically active material is not freeze stable." The examiner failed to identify, and we are unable to find, a portion of Koyama that teaches that the proteinaceous biologically active material is not freeze stable. As appellants point out (Answer, page 15), "[t]he examiner does not address this limitation in the rejection of claim 52 as being anticipated by Koyama...." In this regard, we remind the examiner "[u]nder 35 U.S.C. § 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim." Gechter v. Davidson, 116 F.3d 1454, 1457, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997). "Every element of the claimed invention must be literally present, arranged as in the claim." Richardson v. Suzuki Motor Co., Ltd., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Since the examiner does not address the requirement in claim 53 that the "biologically active material is not freeze stable", and Koyama does not expressly address non-freeze stable biologically active materials, we are compelled to reverse the rejection of claim 52 under 35 U.S.C. § 102(e) as anticipated by Koyama.

Obviousness:

Claims 32-34, 47 and 55-68 stand rejected under 35 U.S.C. § 103 as being unpatentable over Koyama in view of appellants' admitted prior art.

According to appellants (Brief, page 10), claims 32-34, 47, 55, 57, 58 and 61-63 stand or fall together; claims 56 and 68 stand or fall together; claims 64-66 stand or fall together; and each of claims 59, 60 and 67 stand or fall alone.

Accordingly, we limit our discussion to representative claims 55, 56, 59, 60, 64, and 67. Claims 32-34, 47, 57, 58 and 61-63 will stand or fall together with claim 55; claim 68 will stand or fall together with claim 56; and claims 65 and 66 will stand or fall together with claim 64. Young.

Claim 55

The examiner relies on Koyama as set forth above. Answer, page 5. While the examiner finds (Answer, page 4) that Koyama teach that the aqueous polysaccharide-proteinaceous bioactive substance composition can be dried, "either by conventional procedures at reduced pressure and a temperature below 30°C, or else by freeze-drying^[11]," the examiner finds (Answer, page 5), Koyama does "not teach any examples in which conventional drying procedures at reduced pressure and a temperature below 30°C are used." Nevertheless, the examiner asserts (id.),

it would have been obvious to one of ordinary skill in the art at the time [a]pplicants' invention was made to form the dried compositions of Koyama et al[.] using conventional drying

¹¹ See Koyama, column 2, lines 52-56.

procedures at reduced pressure and at a temperature below 30°C^[12] because as admitted by Koyama et al[.], such drying procedures are conventional and are suitable for producing Koyama et al[.]’s desired products, and because as admitted by [a]pplicants at column 1, lines 59-62, of the application, freeze-drying is costly in capital and energy and is irreproducible.

With reference to the Franks Declaration dated October 2, 2000, appellants assert (Brief, page 17), “in 1989^[13], there was no non-freeze drying ‘conventional’ drying procedures carried out at a reduced pressure and temperature below 30°C’ ... used on proteinaceous bioactive compounds.” According to appellants (id.), “[o]ne of ordinary skill in the art in 1989 reading Koyama would have recognized the non-freeze drying language ... as mere surplusage unsupported by any experimental results or process conditions, and therefore would not have been motivated to dry without freeze drying. According to appellants (Brief, page 18),

[e]ven assuming for the sake of argument one of ordinary skill in the art in 1989 was in fact motivated to dry an aqueous unstable material without freeze drying, there was no teaching suggesting using the degree of drying required to obtain a composition that is in a glassy state when existing at 20°C. Because those skilled in the art did not know that the amount of residual water was significant, it is likely that following Koyama’s suggestion to experiment with non-freeze drying would not have resulted in a glassy state material.

In addition, appellants argue (id.),

At best, the passage in Koyama’s reference to a non-freeze drying process ... was a motivation to experiment since (1) it did not identify any process conditions relating to the reduced pressure and temperature (e.g., time of reduced pressure and heat energy

¹² Thereby reaching the requirement of claim 55 wherein a glassy state composition is formed “by evaporating liquid water....”

¹³ Koyama was filed August 31, 1987 and issued April 25, 1989.

to be input to maintain temperature above freezing) that would have resulted in a dry solid containing a proteinaceous bioactive substance ... and (2) it did not relate those process conditions to what was required to achieve the intended stability.

With reference to the Franks Declaration dated October 2, 2000, appellants assert (Brief, bridging sentence, pages 17-18), "one of ordinary skill in the art in 1989 would have believed that drying purified biologically active samples without first freezing them would destroy an unacceptably large fraction of their activity." From this appellants assert (Brief, page 19), "Koyama, provides, at best, a motivation to experiment, not a suggestion to try a specified processing procedure. Moreover, it provides no reasonable expectation of success for a non-freeze dried procedure. For both of these reasons, the obviousness rejections based upon the teachings of Koyama are improper and should be withdrawn."

We agree with appellants, that in order to establish a prima facie case of obviousness, there must be some suggestion or motivation to modify the references or combine reference teachings and a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). We also agree with the examiner (Answer, page 9), "[a]ll the disclosures in a reference must be evaluated ... a reference is not limited to the disclosure of specific working examples." In re Mills, 470 F.2d 649, 651, 176 USPQ 196, 198 (CCPA 1972). In this regard, we note the examiner's argument (Answer, page 10), that Koyama "specifically claim drying the aqueous solution at a temperature below 30°C and reduced pressure (see claim 6), which is further

evidence of the obviousness of such a drying step." Accordingly, we are not persuaded by appellants' assertion that a person of ordinary skill would not have been able to practice Koyama's non-freeze drying process without undue experimentation. In re Michalek, 162 F.2d 229, 231-32, 74 USPQ 107, 109 (CCPA 1947) ("in a patent it is to be presumed that a process, if used by one skilled in the art, will produce the product alleged by the patentee...."). In our opinion, Koyama provides express direction to prepare a dry composition comprising a maltotriose based stabilizer and a biologically active material by evaporating liquid water at a temperature below 30°C and reduced pressure. See e.g., Koyama, claim 6. Therefore, notwithstanding appellants' assertions to the contrary, in our opinion, Koyama provides both the suggestion and a reasonable expectation of success producing a water-soluble dry solid composition by evaporating liquid water at a temperature below 30°C and reduced pressure. Regarding appellants arguments concerning the retention of activity or degree of drying, we agree with the examiner's finding (Answer, page 11), there is no requirement in appellants' claim 55 regarding the retention of a particular amount of activity or that the composition contain a particular amount of water.

For the foregoing reasons we affirm the rejection of claim 55 under 35 U.S.C. § 103 as being unpatentable over Koyama in view of appellants' admitted prior art. As set forth above, claims 32-34, 47, 57, 58 and 61-63 fall together with claim 55.

Claim 56

According to appellants (Brief, page 20),

there is no teaching relied upon by the examiner suggesting, in addition to the limitations discussed above including evaporating liquid water, a method wherein the purified biologically active material is selected from immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide

as required by appellants' claim 56.

The examiner recognizes (Answer, page 6), Koyama does "not teach drying proteins such as enzymes, transport proteins, immunoglobulins, and blood clotting factors." Nevertheless, the examiner asserts (id.),

[i]t would have been obvious to one of ordinary skill in the art at the time [a]pplicants' invention was made to dry proteins such as enzymes, transport proteins, immunoglobins, and blood clotting factors in the methods of Koyama et al[.] because these are known proteinaceous substances which it would be desirable to be able to store and because Koyama et al[.]'s method is applicable to all proteinaceous substances which exhibit a bioactivity in vivo.

We agree.¹⁴ As set forth in In re Rosselet, 347 F.2d 847, 851, 146 USPQ 183, 186 (CCPA 1965). "[t]he test for obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them."

¹⁴ Of interest, we note that appellants' position appears to be in conflict with their position that one of ordinary skill in the art would envision the enzyme "rennin" in their disclosure of a subgenus drawn to "enzymes".

For the foregoing reasons we affirm the rejection of claim 56 under 35 U.S.C. § 103 as being unpatentable over Koyama in view of appellants' admitted prior art. As set forth above, claim 68 falls together with claim 56;

Claim 59

According to appellants (Brief, page 20), there is no teaching in Koyama to suggest evaporating liquid water, or to use "an immunoglobulin" as the biologically active material as is required by appellants' claim 59. For the reasons set forth above, we are not persuaded by appellants' arguments concerning evaporating liquid water. As to the use of "an immunoglobulin" the examiner asserts (Answer, page 12), immunoglobulins "are known substances which like all chemical have to be stored and have to be stored in such a manner so as to maintain their activity." According to the examiner (id.), since Koyama "is applicable to all proteinaceous substances which exhibit a bioactivity in vivo, it would have been obvious to use the process of Koyama ... to store these particular proteinaceous substances." We agree. Accordingly, we affirm the rejection of claim 59 under 35 U.S.C. § 103 as being unpatentable over Koyama in view of appellants' admitted prior art.

Claim 60

According to appellants (Brief, page 20), there is no teaching in Koyama to suggest evaporating liquid water, or to use "a blood clotting factor" as the biologically active material as is required by appellants' claim 60. For the

reasons set forth above, we are not persuaded by appellants' arguments concerning evaporating liquid water. As to the use of "a blood clotting factor" the examiner asserts (Answer, page 12), blood clotting factors "are known substances which like all chemical have to be stored and have to be stored in such a manner so as to maintain their activity." According to the examiner (id.), since Koyama "is applicable to all proteinaceous substances which exhibit a bioactivity in vivo, it would have been obvious to use the process of Koyama ... to store these particular proteinaceous substances." We agree. Accordingly, we affirm the rejection of claim 60 under 35 U.S.C. § 103 as being unpatentable over Koyama in view of appellants' admitted prior art.

Claim 64

According to appellants (Brief, page 20), there is no teaching in Koyama to evaporating liquid water without heating, as required by appellants' claim 64.

In response the examiner asserts (Answer, bridging paragraph, pages 12-13), Koyama "describe conventional drying procedures at reduced pressure and a temperature 'below 30°C.... At such temperatures, there is at best minimal heating involved. Further, the disclosed temperature range renders prima facie obvious the determination of optimum temperatures within the disclosed temperature range, which includes those at which no heating occurs. We agree. Accordingly, we affirm the rejection of claim 64 under 35 U.S.C. § 103 as being unpatentable over Koyama in view of appellants' admitted prior art. As set forth above, claims 65 and 66 fall together with claim 64.

Claim 67

According to appellants (Brief, page 20), “[i]ndependent claim 67 defines a composition that exists in a glassy state at 20°C. Koyama does not suggest [or] disclose storage stable compositions that exist in a glassy state when at 20°C.” For the foregoing reasons, it is our opinion that the examiner has met his burden of setting forth a plausible prima facie case of obviousness. Best. Accordingly, the burden of going forward with evidence or argument was properly shifted to the appellants. In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). However, as the examiner asserts (Answer, page 9), “[a]ppellants have not submitted any probative evidence that Koyama ... do not produce dried compositions in a glassy state, or that Koyama[‘s] ... compositions are not storage-stable at 20°C.” For the foregoing reasons we are not persuaded by appellants’ unsupported arguments. Accordingly, we affirm the rejection of claim 67 under 35 U.S.C. § 103 as being unpatentable over Koyama in view of appellants’ admitted prior art.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART


William F. Smith

Administrative Patent Judge



Donald E. Adams

Administrative Patent Judge

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GRIMES, Administrative Patent Judge, dissenting in part.

I agree with the majority that claim 52 is not anticipated and that claim 39 finds adequate support in the specification while claim 38 does not. I also agree that Koyama supports a prima facie case of obviousness with respect to claims 55, 56, 59, 60, 64, and 67: Koyama suggests stabilizing “proteinaceous bioactive substances” (which reasonably includes immunoglobulins and blood clotting factors) by mixing them with a maltotriose-based polymer and drying them. “Although conventional drying processes carried out at a reduced pressure and a temperature below 30° C are feasible in the invention, freeze-drying is desirable.” Col. 2, lines 52-56.

Thus, Koyama suggests drying under vacuum at temperatures up to 30° C. Even though Koyama prefers freeze-drying, “all disclosures of the prior art, including unpreferred embodiments, must be considered.” Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 807, 10 USPQ2d 1843, 1846 (Fed. Cir. 1989). I therefore agree that Koyama reasonably suggests methods and compositions encompassed by claims 55, 56, 59, 60, 64, and 67.

However, I cannot agree that Koyama anticipates claim 26. Claim 26 is directed to a “glassy state composition.” Appellants’ specification defines a glass as follows:

A glass is defined as an undercooled liquid with a very high viscosity, that is to say at least 10^{13} Pa.s, probably 10^{14} Pa.s or more.

Normally a glass presents the appearance of a homogeneous, transparent, brittle solid which can be ground or milled to a powder. In a glass, diffusive processes take place at extremely low rates,

such as microns per year. Chemical or biochemical changes including more than one reacting moiety are practically inhibited.

Above a temperature known as the glass transition temperature T_g , the viscosity drops rapidly and the glass turns into a rubber, then into a deformable plastic which at even higher temperatures turns into a fluid.

Col. 3, lines 52-64.

“[T]o hold that a prior art reference anticipates a claim, the Board must expressly find that every limitation in the claim was identically shown in the single reference.” Gechter v. Davidson, 116 F.3d 1454, 1460, 43 USPQ2d 1030, 1035 (Fed. Cir. 1997). The limitations can be disclosed expressly or inherently. See Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Koyama does not exemplify any compositions dried under conditions other than freeze-drying: in all of Koyama’s examples, a protein is mixed with a polymer and freeze-dried. See, e.g., col. 3, lines 41-45 (interferon was mixed with various stabilizers, “freeze-dried, and stored at either 4° C or 37° C”). The majority concedes that “Koyama does not use the term ‘glassy state’ to characterize his dry composition.” That is, Koyama does not expressly disclose a “glassy state” composition. Therefore, to find that Koyama anticipates claim 26, the examiner and the majority must have concluded that freeze-drying inherently produces a glassy state composition.

If freeze-dried protein/polysaccharide compositions are inherently in a glassy state, claim 26 is anticipated. See In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (“When the claimed compositions are not

novel they are not rendered patentable by recitation of properties, whether or not these properties are shown or suggested in the prior art.”).

“Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981) (quoting Hansgirk v. Kemmer, 102 F.2d 212, 214, 40 USPQ 665, 667 (CCPA 1939)).

Anticipation, like any USPTO holding of unpatentability, must be established by a preponderance of the evidence. See, e.g., In re Oetiker, 977 F.2d 1443, 1449, 24 USPQ2d 1443, 1447 (Fed. Cir. 1992) (J. Plager, concurring: “In rejecting an application, factual determinations by the PTO must be based on a preponderance of the evidence.”). In this case, that means that the greater weight of the evidence in the record must support a conclusion that the limitation is inherent.

What evidence is cited by the examiner and the majority to show that Koyama’s freeze-dried compositions are inherently in a glassy state? The examiner relies on the “similarity in the components of the compositions and the retained activity of the compositions.” Examiner’s Answer, sentence bridging pages 4 and 5. The majority seems to rely on the same factors. Thus, as I understand it, the examiner and the majority rely on the following evidence:

(1) Both Koyama’s composition and the composition of claim 26 can contain a protein and a maltotriose-based polysaccharide;

(2) both compositions are dried; and

(3) both are storage-stable.

I do not agree that the evidence of record is adequate to show that Koyama's compositions are inherently in a glassy state. The instant specification discusses freeze-drying as a known technique for stabilizing proteins. See col. 1, lines 49-66:

The commonest method for the stabilisation of isolated protein preparations is freeze-drying. . . . The aqueous isolate of the active material in a suitable pH buffer and in the presence of a cryoprotectant is first frozen, typically to -40° to -50° C.; the ice is then removed by sublimation under vacuum and at low sub-zero temperatures, following which the residual moisture which may amount up to 50% of the "dried" preparation is removed by desorption during which the temperature gradually rises. . . . Exposure [of the freeze-dried protein] to ambient temperatures for periods of days to weeks can result in significant activity losses.

The specification goes on to distinguish the disclosed method of making glassy state compositions from freeze-drying. See col. 2, lines 21-23 ("There would furthermore be advantage in providing a more cost effective process than the current freeze-drying process.") and col. 2, lines 60-61 ("A further feature is that the process is energy efficient, requiring much less energy than freeze-drying."). The specification also distinguishes between the compositions resulting from the disclosed method and from freeze drying. See col. 4, lines 23-29 ("[I]f the T_g of the composition is close to or below room temperature it may be necessary or desirable to refrigerate the glassy composition if storage is for a prolonged period. This is less convenient but still is more economical than freeze-drying.").

Appellants' specification discloses two methods of making glassy state compositions. Koyama's process is more similar to the second of the two

processes (col. 6, lines 29-58). In that process, the active material (e.g., protein) is mixed with the carrier substance (e.g., polysaccharide) and the resulting solution is divided into smaller aliquots. These aliquots are then dried under reduced pressure “at a temperature not exceeding 40° C, preferably in the range of 20 to 30° C . . . for some hours, for instance 24 to 36 hours.” The specification provides an example of applying this process to a composition containing lactate dehydrogenase and several different carriers, including dextran. See Example 13 (column 13). In that example, the enzyme- and dextran-containing composition showed 102% residual activity after 8 weeks at 25° C. See the table in col. 13. Koyama’s Example 1-B shows that a freeze-dried composition containing dextran and human interferon retained only 81.5% activity after two months at 4° C and 65.3% activity after two months at 37° C. See Table I.

The majority plays down the significance of the 8-week measurements disclosed in Appellants’ specification, focusing instead on the activity measurements at other time points and finding it “curious” that neither Appellants nor I discuss the activity measured at weeks 2 and 4. The reason for that is simple – Koyama only measured residual activity after 2 months’ storage. The only data in the specification that can be meaningfully compared to the prior art, therefore, are the 8-week storage data.

In sum, the evidence shows that Appellants’ specification describes the disclosed process of making glassy state compositions as an alternative to, and therefore different from, freeze-drying. Appellants’ specification also describes

glassy state compositions as stable when stored at room temperature and therefore “more economical than freeze-drying” which requires storage at -20° C. Finally, Appellants’ specification shows that a glassy state composition containing a protein and dextran is more stable at room temperature (25° C) than a freeze-dried one is when stored refrigerated (4° C). I do not agree that a preponderance of the evidence in the record supports the conclusion that Koyama’s composition is inherently in a glassy state. Therefore, it is premature to shift the burden of proof to applicants and make them show that the claimed composition differs from those in the prior art. I would reverse the rejection under 35 U.S.C. § 102.



Eric Grimes
Administrative Patent Judge

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